Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 9-18, 32 and 33 are pending in the application, with claims 9, 10, 12 and 33 being the independent claims. Claims 10, 12 and 33 have been amended to recite specific neoplastic disorders listed in a Markush group. Support for the amendments to claims 10, 12 and 33, can be found, *inter alia*, in Examples 1 and 2 at pages 85-90 of the specification. Claims 10 and 12 have been amended such that they recite "binds to" rather than "associates with" to make explicit what is implicit in the claims. Support for amended claims 10 and 12 can be found, *inter alia*, in the specification at ¶ 70. Claim 18 has been amended to in order to provide proper antecedent basis for the claim. Support for claim 18 can be found in claim 18 as originally filed. Support for these changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Elections/Restrictions

Applicants note the Examiner's comments related to Applicants' election with traverse of Group II (claims 9-18 and 32-33) with SEQ ID NO: 2.

Information Disclosure Statement

Applicants thank the Examiner for consideration of the submitted Information Disclosure Statements (IDSs), submitted on November 10, 2004 and January 20, 2006.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 9, 12-18 and 32 were rejected under 35 U.S.C. § 112, second paragraph, for allegedly "failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." (Office Action, Page 3.) Specifically, the Examiner stated:

> [c]laims 9 and 12-18 are vague and indefinite because the term 'associates with IGSF9' in the claims 9 and 12 is not clear. It cannot be determine what the meaning of 'associates with IGSF9' is. Does it mean to bind to IGSF9 protein or not?

(*Id.*)

In order to expedite prosecution, but without acquiescing to the Examiner's rejection, Applicants have amended claims 9 and 12 such that they recite "binds to" rather than "associates with" to make explicit what is implicit in the claims.

Applicants assert that one of ordinary skill in the art would readily understand that the meaning of the term "associates with," with respect to an antibody or an antigen binding fragment, means "to bind to" or "to come into physical contact with." The ordinary meaning of the term "associates with" means "to join," where "join applies to the physical contact or union of at least two separate things . . . . " The American Heritage Dictionary, Fourth Edition (2000). Furthermore, one of ordinary skill in the art

would readily understand that an antibody is an immunoglobulin molecule that contains an antigen binding fragment. The meaning of the term "antigen binding fragment" is clear on its face and clear to one of ordinary skill in the art; that is, an antigen binding fragment is a fragment that binds to an antigen. Thus, the meaning of "associates with" in view of an antibody, or antigen binding fragment, means "to bind to," or "to come into physical contact with."

In addition, the specification provides ample guidance for the meaning of the term "associates with." Specifically, the specification states that "[t]he modified antibodies of the present invention *preferably associate with, and bind to*, IGSF9 or LIV-1." (Specification, ¶ 70 (emphasis added).) Thus, the specification uses the terms "associate with" and "bind" interchangeably.

Accordingly, Applicants respectfully request that the rejection of claims 9 and 12 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 10-18 and 33 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. (Office Action, Pages 3-4.) In particular, the Examiner has alleged that "the specification does not provide a method of treating any cancer with any agent, which could bind to IGSF9 comprising an antibody to IGSF9 (SEQ ID NO:2)." (Office Action, Page 4.) Furthermore, the Examiner stated that "[t]here are no working examples to guide or assist the skilled artisan in practicing the claimed method of treating any neoplastic disorder with antibody or binding fragment to IGSF9." (*Id.*)

In order to expedite prosecution, but without acquiescing to the Examiner's rejections, Applicants have amended claims 10, 12 and 33 to recite specific neoplastic disorders recited in a Markush group. Support for the amendments to claims 10, 12 and 33, can be found, *inter alia*, in Examples 1 and 2 at pages 85-90 of the specification.

In order for a claim to be enabled, the specification must teach one of ordinary skill in the art to make and use the invention without undue experimentation. The factors that can be considered in determining whether an amount of experimentation is undue have been set forth in *In re Wands*, 858 F.2d731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: 1) the guidance provided by the specification; 2) the amount of pertinent literature; 3) the presence of working examples; and 4) the predictability of the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine. *See id.*

Enablement is not precluded if some experimentation is required so long as it is not "undue." *In re Wands*, 585 F.2d 731, 737 (Fed. Cir. 1988). In *Wands*, the court held that a specification was enabling for obtaining antibodies needed to practice the invention because it contained considerable guidance, there was a high level of skill in the art, and all methods to needed to practice the invention were well known. Applicants note that obtaining antibodies is not a trivial exercise, but yet it was considered routine.

In the present case, as in *Wands*, a person of skill in the art for the claimed invention has a doctorate or equivalent and would be able to prepare an antibody for use in the claimed method. First, experiments have been performed identifying which types of tumors have increased expression of IGSF9. (*See* Specification, Examples 1 and 2.)

Furthermore, a working example in the specification describes the preparation of a monoclonal antibody that specifically binds to IGSF9. (*See id.*, Example 4) In addition, the specification describes the use of a monoclonal antibody to IGSF9 to detect IGSF expression levels in tumor samples. (*See id.*, Example 5) Furthermore, acceptable treatment alternatives are known to those skilled in the art, including, but not limited to, observation, mode of surgery, non adjuvant therapies such as radiation, and adjuvant therapies such as tamoxifen or cytotoxic chemotherapy. *See* Specification, ¶ 296. Thus, like in *Wands*, the skill in the art is high, the specification provides ample guidance and applicable methods are known to one of ordinary skill in the art.

The Examiner describes several articles, including Jain R.K. (*Scientific American, 271*: 58-65 (1994)) (Jain), Dillman, R.O. (*Annals of Internal Medicine, 111*: 592-603 (1989)) (Dillman I), Weiner, L.M. (*Seminars in Oncology, 26* (4 Suppl 12): 41-50 (1999)) (Weiner) and Dillman, R.O. (*Journal of Clinical Oncology, 12*:1497-1515 (1994)) (Dillman II) which discuss the use of antibodies in the treatment of cancers. Each of these articles, which the Examiner uses to support the arguments related to enablement, is not representative of the state of the art of the present invention. In fact, Dillman I predates the priority date of the present application (*i.e.* January 27, 2003) by nearly 9 years. The most current article cited by the Examiner, Weiner, was published in 1999, and predates the priority date of the present application by 4 years. Thus, the Examiner has not provided a single reference to support an argument that reflects the state of the art of the present invention. Thus, the Examiner has failed to establish a *prima facie* case of lack of enablement.

Furthermore, Applicants assert that although the articles disclose obstacles in treatment, they also support the use of monoclonal-antibody based therapeutics in the treatment of cancer. For example, the first sentence in Weiner states

> [m]onoclonal antibody-based therapeutics are beginning to realize the promise that was predicted with the advent of the core technology more than 20 years ago. Antibody-based therapeutics targeting tumor cell surface antigens such as B-cell idiotypes, CD20 on malignant B cells, CD33 on leukemic blasts, and HER2/neu on breast cancer cells have shown efficacy in recent clinical trials. Multiple antibody-based strategies have shown promising efficacy in recent clinical trials.

Weiner, Abstract. Applicants note that, like the surface antigens described above, IGSF9 is also expressed on the cell surface, and thus more accessible to antibody-binding, and to antibody-based therapeutics. Weiner further states that "[t]he results of these studies clearly demonstrate that antibody-based molecules that specifically target cancer have important therapeutic use." Weiner, Page 42, Col. 1. Weiner also discloses Table 5, which lists several studies showing promising results using monoclonal antibody therapy and concludes that "[t]he initial clinical studies using antibodies and their derivatives have identified a number of areas that promise to make significant impacts in the management of patients afflicted by cancer (Table 5)." Weiner, Page 49, Column. 1. Thus, the Weiner article not only lists promising results in the treatment of cancer, but also provides guidance to one of skill in the art as to how best to carry out antibody-based therapy for the treatment of cancer.

Based on the arguments presented above, Applicants assert that the Examiner has not established a *prima facie* case of lack of enablement. Furthermore, Applicants assert that the specification provides sufficient guidance for one of skill in the art to make and use the claimed invention. Accordingly, Applicants respectfully request that the rejection of claims 10-18 and 33 under 35 U.S.C. § 112 be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 102

Claims 9-18 and 32-33 were rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by either Hoefnagel *et al.* (*Eur. J. Nucl. Med. 28*: 359-68 (2001)) (Hoefnagel). Specifically, the Examiner asserted that

> Hoefnagel et al., teach a method of treating neuroblastoma in mice with an antibody to an immunoglobulin superfamily member *L1-CAM* (abstract) expressed in the brain tissue. Hoefnagel et al., also disclose that the *anti-L1-CAM antibody, mAB chCE7*, is Iodine-131 labeled an the antibody specifically binds to brain tissue, not other tissue such as kidney. Hoefnagel et al., further disclose that the tumors were treated with single injection of *131I-mAB chCE7* and after the therapy the subcutaneous tumors nearly disappeared (abstract).

(Office Action, Pages 6-7. (emphasis added).)

Applicants note that a claim is anticipated if each and every limitation of the claim is recited in a single prior art reference. *Nystrom v. Trex Co.*, 374 F.3d 1105, 1117, 71 U.S.P.Q.2d 1241, 1250 (Fed. Cir. 2004); *Merck & Co. v. Teva Pharmaceuticals USA, Inc.*, 347 F.3d 1367, 1372, 68 U.S.P.Q.2d 1857, 1861 (Fed. Cir. 2003)("An

'anticipating' reference must describe all of the elements and limitations of the claim in a single reference, and enable one of skill in the field of the invention to make and use the claimed invention.").

Hoefnagel, as noted by the Examiner, describes the molecule L1-CAM, and also describes a monoclonal antibody of L1-CAM, designated mAB cHCE7. L1-CAM is a different molecule than IGSF9, as recited in claims 9-18 and 32-33. Thus, Hoefnagel clearly does not disclose each and every limitation of the claimed invention. As noted above, in order for a reference to be anticipating, it must teach or suggest *every element of the claimed invention.* Because none of the pending claims are anticipated by Hoefnagel, Applicants respectfully request that the rejection under 35 U.S.C. § 102 be withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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